CALIFORNIA INSTITUTE OF TECHNOLOGY

DIVISION OF BIOLOGY 156-29
FAX: (818) 449-0756

9 February 1990

Dr. Joshua Lederberg
The Rockefeller University
1230 York Avenue
New York, N.Y. 10021-6399

Dear Dr. Lederberg:

I am sorry for the delay in answering your note. Thank you for your reprints and for calling my attention to Lettré's paper. I had some trouble in locating the old issue of ***Zeitschrift für Krebsforschung*** containing this paper. I was certainly familiar with your long-standing interest in cytoplasmic inheritance. Lettré's observations are difficult to interpret. Uptake of mitochondria into mammalian cells by endocytosis has been well documented (see Nass, ***Science* 165**, 1128-1131, 1969, and Clark and Shay, ***Nature* 295**, 605-607, 1982). Clark and Shay have claimed that under certain conditions, involving selection of a chloramphenicol resistance marker, mitochondria taken up by endocytosis may establish their DNA in the host cell. Unfortunately, such experiments have not been followed up, nor has the establishment of exogenous mtDNA been unambiguously proven by RFLP, although the senior author (Shay) has continued to be active in the general area of somatic cell genetics of mtDNA. In Lettré's experiments, there may have been a selection of cells which had reacquired their respiratory capacity by uptake of functional mitochondria. Alternatively, there may have been a recovery of damaged mitochondria in the intact cells which was favored by some component in the homogenate distinct from intact mitochondria.

We are certainly alerted to the possibility that ethidium bromide may have had mutagenetic effects on nuclear DNA, in addition to the inhibitory action on replication of mtDNA. Our initial ρ° cell variants (derived from the 143B cell line) have two identified biochemical defects (described in the ***Science*** paper), both of which can be accounted for by the lack of a functional respiratory chain. In the presence of uridine and pyruvate, the ρ° cells grow at a rate almost identical to that of the parental line. We are currently characterizing in more detail these ρ° cell lines. We shall be glad to send you preprints of this work as soon as they are ready. We have recently isolated another ρ° human cell line different in genetic origin from the 143B derivatives, which also exhibits the uridine and pyruvate auxotrophy. The focus of our work is presently on using these ρ° cell lines to investigate nucleo-mitochondrial interactions in human cells in a "normal" or pathological context.

With best regards,

Sincerely yours,

Giuseppe Attardi

Giuseppe Attardi

GA:sc

PASADENA, CALIFORNIA 91125

ne p-47